REMARKS

Reconsideration of this application is respectfully requested.

Applicant has amended claim 52. The amendment adds no new matter. Claims 42-57 are pending in this application. A marked-up version showing changes made to claim 52 is attached.

Rejections under 35 U.S.C. § 101

Claims 42-57 were rejected under 35 U.S.C. § 101 for allegedly lacking utility. Applicant traverses the rejection.

Applicant's claimed invention fulfills the requirements of 35 U.S.C. § 101. In contrast to the Examiner's position, specific utilities need not have been established. Otherwise, we would not speak of "asserted utilities."

As the Office has recognized, IL-1 delta exhibits high identity with IL-1ra and other IL-1 family members. (Paper No. 12 at 8.) Since IL-1 family members are involved in modulating inflammation, the skilled artisan would expect that IL-1 delta is also involved in modulating inflammation. Applicant asserted that IL-1 delta is useful for probes to identify nucleic acid encoding proteins having IL-1 delta activity. (Specification at 36, lines 4-5.) Due to the RNA expression pattern of IL-1 delta, probes based on the DNA sequence of SEQ ID NO:3 can be used to detect lymph node, thymus, tonsil, brain placenta, lung, skeletal muscle, prostate, and testis tissue and cell types by methods such as *in situ* hybridization. (*Id.* at 36, lines 28-30). Similarly, antibodies raised against IL-1 delta polypeptides can be used to detect lymph node, thymus, tonsil, brain placenta, lung, skeletal muscle, prostate, and testis tissue and cell types by conventional immunohistochemical methods. (*Id.* at 57, lines 9-15). In

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addition, all or a portion of the nucleic acids of SEQ ID NO:3, including oligonucleotides, can be used by those skilled in the art in well-known techniques to identify human chromosome 2, to analyze abnormalities associated with gene mapping to chromosome 2, to distinguish conditions in which this marker is rearranged or deleted, and as a positional marker to map other genes of unknown location. (*Id.* at 37, lines 1-32.)

In contrast to the Office's position, the asserted utilities are specific. A "specific utility" is specific to the subject matter claimed. M.P.E.P. § 2107.01 at p. 2100-32, col. 1. In contrast, a "general utility" is one that is applicable to the broad class of the invention. *Id.* Applicant's asserted utilities are not applicable to the broad class of the invention, but are specific to the claimed subject matter. That is, all polynucleotides would not be useful for Applicant's asserted utilities. For example, all polynucleotides could not detect the 2q11-12 region of chromosome 2 or the specific RNA detected by Applicant. The Office has not disputed this. Similarly, all polynucleotides could not detect RNA expression in lymph node, thymus, tonsil, brain placenta, lung, skeletal muscle, prostate, and testis tissue and cell types by methods such as *in situ* hybridization. The Office has not disputed this.

Furthermore the Office's assertion that "many probes such as SEQ ID NO:3 would be equivalent to the instant probes in localizing this region" (Paper No. 12 at 6) is unsupported and does not provide an adequate basis for the Office's conclusion that Applicant's utilities are not specific. Even if other probes existed that were equivalent, this is not the legal standard for determining whether Applicant's probes have utility. Applicant's are unaware of any legal standard that would require Applicant's invention to be unique in producing a certain result. An asserted utility need not be a novel utility.

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Rather, Applicant's invention must not solely have a utility that is "throw-away," "insubstantial," or "nonspecific," such as being used as landfill. (*See* M.P.E.P. § 2107 at p. 2100-29, col. 2.) Applicant's asserted utilities are not throwaway, insubstantial, or nonspecific, but are specific to the claimed subject matter.

In addition, the M.P.E.P. supports the utility of Applicant's invention. M.P.E.P. § 2107.01 indicates that "a claim to a polynucleotide, whose use is disclosed simply as a 'gene probe' or 'chromosome marker,' would not be considered to be specific ***in the absence*** of a disclosure of a specific DNA target." M.P.E.P. § 2107.01 at p. 2100-32, col. 1 (emphasis added). This statement implies that ***in the presence*** of a disclosure of a specific DNA target, a claim to a polynucleotide, whose use is disclosed simply as a "gene probe" or "chromosome marker" would be considered to be specific. Were this implication not true, the sentence would read, "a claim to a polynucleotide, whose use is disclosed simply as a 'gene probe' or 'chromosome marker,' would not be considered to be specific," period. Of course, such a blanket rule was not intended by the PTO, which clearly contemplated the disclosure of a specific DNA target supporting a specific utility as a gene probe or chromosome marker. Applicant's specification discloses a specific DNA target (human chromosome 2) and specific RNA targets (in lymph node, thymus, tonsil, brain placenta, lung, skeletal muscle, prostate, and testis tissue) Thus, Applicant's disclosures of using IL-1 delta as a "gene probe" and as a "chromosome marker" are specific utilities.

The above-statement from the M.P.E.P. is also inconsistent with the Office's position that "[u]se of a polynucleotide as a tissue specific probe, or a chromosomal marker is not considered a specific and substantial utility, because almost every

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polynucleotide exhibits some tissue specific pattern of expression . . . ." (Paper No. 12 at 5.) Illustrating the Office's attempt in Paper No. 12 to create a blanket rule against gene probe or chromosome marker specific utilities where the M.P.E.P. clearly contemplates such asserted utilities being specific in some cases, the Office Action ignores the caveat "***in the absence*** of a disclosure of a specific DNA target." This is improper since Applicant has disclosed a specific DNA target on human chromosome 2. Furthermore, a "tissue ***specific*** pattern of expression" must be considered **specific**. The use of the word "specific" negates any conclusion to the contrary.

Applicant has asserted a variety of utilities for the claimed invention. Undoubtedly, Applicant's invention is not totally incapable of achieving a useful result. Consequently, Applicant's claimed invention cannot be rejected for lacking utility. *See Brooktree Corp. v. Advanced Micro Devices, Inc.*, 24 U.S.P.Q.2d 1401, 1412 (Fed. Cir. 1992)("to violate [the utility requirement of] § 101 the claimed device must be totally incapable of achieving a useful result"). Accordingly, Applicant respectfully requests withdrawal of the rejection.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 42-57 were rejected under 35 U.S.C. § 112, first paragraph, for allegedly not having either a specific and substantial asserted utility or a well established utility for the same reasons set forth for the rejections under 35 U.S.C. § 101.

Applicant traverses the rejection. For the reasons detailed above, the skilled artisan would understand how to use the claimed invention. Accordingly, Applicant respectfully requests withdrawal of the rejection.

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Claims 42-57 were rejected under 35 U.S.C. § 112, first paragraph, because the specification allegedly does not reasonably provide enablement for a nucleic acid molecule that encodes a fragment of the polypeptide of SEQ ID NO:4, wherein the fragment binds to cells expressing an IL-1 delta receptor; or an isolated nucleic acid molecule that encodes a polypeptide that comprises an amino acid sequence that is at least 80% identical to SEQ ID NO:4, wherein the polypeptide binds to cells expressing an IL-1 delta receptor; or a nucleic acid molecule that hybridizes to the nucleic acid molecule of SEQ ID NO:3, wherein said nucleic acid molecule is at least 90%, 95%, 98%, or 99% identical to SEQ ID NO.3; or a nucleic acid molecule, wherein the nucleic acid molecule comprises at least 30 contiguous or 60 contiguous nucleotides of the nucleic acid molecule of SEQ ID NO:3. The Office concludes that Applicant's specification does not enable the skilled artisan to make the invention commensurate in scope with the claims. (Paper No. 12 at 7.) It is the Office's position that the claims are drawn to a large number of different molecules. The Office concedes that the skilled artisan could make these molecules and test their binding. (Paper No. 12 at 10.) However, the Offices concludes that this would require undue experimentation because there is no guidance regarding which of the molecules would retain the function screened for. (*Id.*)

Applicant traverses the rejection. First, claims 56 and 57 are not limited to nucleic acids that encode a polypeptide that binds to cells expressing an IL-1 delta receptor. Rather, claims 56 and 57 encompass nucleic acids without regard to the ability of any encoded polypeptide to bind to cells expressing an IL-1 delta receptor. The identity of the encoded polypeptide is not a limitation of these claims. The Office

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has not given any reasons that undue experimentation would be required to make the invention of claims 56 and 57. None of the Office's reasons for non-enablement are relevant to claims 56 and 57. Since no reasons have been given to support the rejection with respect to claims 56 and 57, the inclusion of these claims in the rejection is in error. *See In re Wright*, 27 U.S.P.Q. 2d 1510, 1515 (Fed. Cir. 1993) (indicating that "the PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the specification of the application . . . ."). *See also* 37 C.F.R. § 1.104(a)(2)("The reasons for any adverse action . . . will be stated in an office action and such information or references will be given as may be useful in aiding the Applicant . . . .")

Second, routine screening for molecules cannot be equated with undue experimentation. *See In re Wands*, 8 U.S.P.Q.2d 1400, 1406 (Fed. Cir. 1988). The Office has conceded that the skilled artisan could make the claimed molecules and screen for their binding. (Paper No. 12 at 10.) The fact that some screening, even a very large amount of screening, is required cannot serve as the basis for concluding that undue experimentation is required. *See In re Wands*, 8 U.S.P.Q.2d at 1406. Accordingly, Applicant respectfully requests withdrawal of the rejection.

Furthermore, Applicant provides detailed guidance as to how one skilled in the art should be selecting the polypeptide variants on pages 17-24 of the specification. For example, a given amino acid may be replaced by a residue having similar physiochemical characteristics. (Specification at 18, lines 12-18.) As the Office has recognized, IL-1 delta exhibits high identity with IL-1ra and other IL-1 family members.

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(Paper No. 12 at 8.) As further recognized by the Office, for proteins whose sequence identity is above 30%, one can use homology modeling to build structure. (Paper No. 12 at 10, citing Skolnick et al.) Since all of the IL-1 family members are involved in modulating inflammation, the skilled artisan could compare the sequences of the IL-1 family members to predict likely positions within IL-1 delta that would not affect binding. Screening for binding activity of IL-1 polypeptides modified at these positions could be used to confirm these predictions.

With respect to the Office's assertion (Paper No. 12 at 9) that Smith et al. disclose a lack of minimum measurable activity, Applicant notes that the results of Smith et al., relate to the binding of IL-1 family members to immunoglobulin Fc fusion proteins of known IL-1 receptor family members (Smith et al., page 1171, paragraph labeled "Receptor Binding Assays" and page 1174, first paragraph of column 2). Smith et al. discuss these results on page 1175, in the first complete paragraph of the first column, where they postulate that there could be unknown IL-1 receptor family members to which the tested IL-1 family members bind, that high affinity binding may require the presence of two receptor subunits, or that binding may occur through a different type of receptor. Applicant respectfully notes that the present claims do not recite binding to an immunoglobulin Fc fusion protein, but to cells expressing an IL-1 delta receptor.

Moreover, the ability to determine binding to such cells is within the ability of one of ordinary skill in the arts, as shown in Debets et al., (*J. Immunol.*, 2001, 167:1440-1446, Exhibit 1). Debets et al. evaluated the activity of IL-1 delta and IL-1 epsilon (another IL-1 family member) on Jurkat cells (see, page 1141, "Reporter Assay"). They found that neither IL-1 delta nor IL-1 epsilon activated NFkappaB via the classic

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members of the IL-1 receptor family (paragraph spanning pages 1142 and 1143), but that IL-1 epsilon signaled via the orphan IL-1 receptor-like molecule IL-1R6, and that IL-1 delta antagonized this signaling (page 1443, column 1). These authors stated that they did not find their results to contradict those of Smith et al., noting that use of immunoglobulin Fc fusion proteins might not allow detection of binding when a second receptor is required for affinity conversion and detectable binding (page 1145, paragraph spanning column 1 and 2). Thus, those of ordinary skill in the art are able to measure the activity of IL-1 delta through routine experimentation. Binding to cells expressing an IL-1 delta receptor is a measurable activity. No undue experimentation would be required. Accordingly, Applicant respectfully requests withdrawal of the rejection.

Applicant submits that this application is in condition for allowance. If the Examiner should disagree, the Examiner is invited to contact the undersigned to discuss any remaining issues.

If there is any fee due in connection with the filing of this paper, please charge the fee to our Deposit Account No. 06-0916.

Respectfully submitted,

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Marked-Up Version Showing Changes Made to Claim 52

52. (Amended) A nucleic acid molecule that hybridizes to the nucleic acid molecule of SEQ ID NO:3, wherein the hybridization conditions include 50% formamide and 6XSSC, at 42°C with washing conditions of 60°C, 0.5XSSC, 0.1% SDS, wherein said nucleic acid molecule is at least 90% identical to SEQ ID NO:3 and further wherein the nucleic acid molecule encodes a polypeptide that binds to cells expressing an IL-1 delta receptor.

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